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THE  
PHYSIOLOGICAL ACTION  
OF  
NITROUS OXIDE GAS,

AS SHOWN BY EXPERIMENTS UPON  
MAN AND THE LOWER ANIMALS.

TOGETHER WITH SUGGESTIONS AS TO ITS  
SAFETY, USES AND ABUSES.

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BY  
J. J. COLTON, A.M., M.D.  
PHILADELPHIA, PA.

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1871.

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THE  
PHYSIOLOGICAL ACTION  
OF  
NITROUS OXIDE GAS.

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It has been a disputed point among scientific men, ever since the protoxide of nitrogen came into general use as an anæsthetic, whether its action depends upon oxidation or whether the carbonic acid generated either by the ordinary disintegration of tissue, or by superoxidation, produces the anæsthesia. Eminent gentlemen in this country and Europe have maintained (and with some plausibility) that carbonic acid, by its action upon the nervous-centres, produces the anæsthesia, arriving at this conclusion from the fact that evidences of asphyxia are, in some cases, so manifest, while others have held to the theory of oxidation.

Having administered this gas to many thousands of persons, having inhaled it in my own person, hundreds of times during as many successive days, and having carefully watched its effects upon the system under the greatest variety of circumstances and conditions, I have maintained that its action must depend upon oxidation, and that the indications of asphyxia (slight in ordinary cases) are merely an incidental effect rather than the main cause of anæsthesia.

The following facts and experiments, it seems to me, clearly establish this theory :

Exp. 1. Take two jars of equal size filled with lime water, pass a definite amount of air, as it comes from the lungs, through one solution, and it is rendered turbid ; pass an equal amount of nitrous oxide, as it escapes from the lungs, through the other solution, and it is also rendered turbid, but to a greater degree than the first, indicating the presence of carbonic acid in greater quantity.

Exp. 2. Breathe through a tube into a solution of litmus blue, and it is changed to red. It will take, we will say, 15 seconds to effect the change (the time depending upon the strength and quantity of the solution). Now breathe nitrous oxide gas through another solution of the same strength and quantity, and we shall notice the change of color in from 10 to 12 seconds, indicating the elimination of carbonic acid to a greater extent than the normal amount, while breathing the gas, as in the first experiment.

Exp. 3. Take a full inspiration of air, retain it in the lungs for one minute, and there are no indications of anæsthesia. Now try the same experiment with the gas, and the anæsthetic effect is manifest almost to insensibility while there are no indications of asphyxia.

We have thus demonstrated, by the first two experiments, that while breathing protoxide of nitrogen, an increased amount of carbonic acid is exhaled, and as this excess *must* be produced by oxidation, we *reasonably* infer that the action of the protoxide is oxidation ; and the third experiment furnishes corroborative testimony, though of a negative character ; for if the retention of carbonic acid cause the anæsthesia, why are there not some indications when air is retained in the lungs ?

If we inhale pure nitrogen, we still exhale carbonic acid for a time, owing to the union of the oxygen previously introduced into the system, with the carbon and hydrogen of the tissues, but the amount is sensibly diminished. Now, this diminished amount of carbonic acid might have been anticipated, since we have not furnished sufficient oxygen to produce the normal

amount. But, on the other hand, when we find an increased amount of carbonic acid, we infer a corresponding increase of oxidation.

But it is objected that nitrous oxide is not a mixture of gases like the air, but a chemical compound, and therefore it does not act by oxidation. Let us see. Exp. 4. Plunge a lighted taper into the gas, and it burns with greatly increased brilliancy; the heated elements of the taper presenting a stronger affinity for the oxygen than the nitrogen does, take it and form the new combinations, carbonic acid and water. This fact shows the affinity of the elements comprising nitrous oxide to be feeble.

Reasoning, now, from analogy, we might be led to infer that similar results would follow the introduction of the gas into the system, and such we find to be the case. The oxygen of the gas, by its stronger affinity, seizes upon the carbon and hydrogen of the tissues, with the same results of combination as in the case of the taper; in other words, we have superoxidation.

But it is objected that *pure oxygen* exerts a less powerful action upon the system than the gas which is two-thirds nitrogen. The answer is simply, that the blood absorbs but a small percentage of oxygen, so that when it is introduced into the lungs it finds its way into the system slowly, while nitrous oxide is rapidly absorbed and conveyed to the tissues to be given up for combination.

Exp. 5. If one takes a full inhalation of the gas, he instantly feels a thrill throughout the entire system. This is the incipient stage of anæsthesia, and the rapidity of its action is another proof of the theory of oxidation; for if these sensations were caused by the accumulation of carbonic acid, we should hardly anticipate such a result in the course of a few seconds.

It is still further objected that the asphyxiated appearance of persons under its influence, indicating a superabundance of carbonic acid in the system, suggest, at least, that it is the cause of anæsthesia. The third, fourth, and fifth experiments furnish proof of the absurdity of this conclusion.

Moreover, the principle evidence of asphyxia ordinarily manifested is the cyanosed tint of the lips, which is, in part, pro-

duced by pressure in holding them tightly upon the inhaling tube, while in certain cases, in which these evidences are more striking, there is a cessation of breathing caused by the tongue falling back upon the epiglottis; by removing this obstruction, and allowing the patient a breath of air, the symptoms of asphyxia disappear. If the inhalations be prolonged to extreme limits, we shall also notice the asphyxiated appearance owing to the accumulation of carbonic acid.

The above indications furnish the main argument in favor of the carbonic acid theory. That there accumulates in the system a larger than the normal amount of carbonic acid is evident, and this is entirely consistent with the theory of oxidation, but this accumulation is not in sufficient amount in ordinary cases to attract attention, certainly not enough to produce profound insensibility. Moreover, the effects of nitrous oxide upon the system are not such as we should anticipate, were they caused by the action of carbonic acid, for it is depressing in its influence. Even if a slight impediment is offered to its elimination from the lungs, "a feeling of discomfort and depression increasing with the duration of the interruption is speedily felt."

Now, while inhaling the nitrous oxide, although there is an increase of carbonic acid in the system, yet, if it be in sufficient amount to produce anaesthesia, how shall we explain the immediate reaction, and the agreeable sensations while inhaling, as well as for some time subsequent.

In the ordinary use of stimulants, there follows "a period of depression corresponding to the exaltation of the functions excited," yet persons who have submitted to the influence of nitrous oxide give no indications of this character. On the contrary, there ordinarily follows a period of exhilaration, just what might be anticipated from an excess of oxygen.

The system resumes its normal condition as soon as the oxygen has been disposed of by union, and the carbonic acid and other products of oxidation eliminated, which process is very rapid—while chloroform, ether, alcohol, and other narcotics and stimulants linger in the system much longer, and by their prolonged

action upon the nervous-centres, produce their depressing effects and obstruct oxidation.

But the wonderful power of the nitrous oxide yet remains to be explained.

It is a well-known principle of chemistry, that elements in the nascent state, just liberated from union, exhibit remarkable characteristics and properties.

Nitrogen and hydrogen, for example, placed in a jar together, manifest no affinity for each other, and cannot be induced to unite even by the application of the most intense heat—but let them come together just at the moment of liberation from other compounds, and they combine with the utmost avidity. This is the precise condition in which the oxygen of the protoxide is found, as it enters into combination with the tissues of the body—just liberated from its union with nitrogen, it is in its nascent state—the active condition, and thus it exhibits its extraordinary powers of oxidation.

I have in this brief and cursory manner endeavored to prove, (1) that persons breathing protoxide of nitrogen exhale a larger amount of carbonic acid than while breathing common air; and (2) that its action is essentially oxidation, and that the excess of carbonic acid in the system is merely incidental, and in no wise sufficient to produce anæsthesia; and, (3) that its inoffensive effects are due to its action as an oxidizer; and (4) that no subsequent depression follows, but rather a rapid reaction; because, acting by oxidation, the products of its combinations are speedily eliminated from the system; and, (5) that its remarkably powerful action is due to its entering into new combinations, just at the moment of its liberation, when in its nascent state. I shall reserve for a future article what I had intended to say of its uses and abuses, and close by expressing my profound conviction that the pure protoxide of nitrogen, administered within proper limits, is harmless in its action; while, if made from contaminated materials; if generated at too high a temperature; if used immediately after it is made; if the impurities ordinarily found in it be not removed; if inhaled in sufficient quantity to produce profound anæsthesia, after being prepared for a

few days, or if the administration of the *pure gas* be persisted in beyond *certain limits*, it is capable of an immense amount of mischief. I would also express the hope that a free and full discussion of the subject may afford a better knowledge of its physiological action and increase its value as an agent for the relief of human suffering.

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The foregoing was published in the *Medical and Surgical Reporter* of July 2d, 1870. Since that time I have, by a series of experiments, been enabled to furnish additional proofs of the above propositions, and I shall *now* endeavor to show that anæsthesia is produced by oxidation in the systemic capillaries, instead of by a want of oxidation upon the brain, as is the case with chloroform.

In order to verify with greater accuracy the fact of an increase of oxidation, I have ascertained the exact *weight* of carbonic acid in a given quantity of air, as it comes from the lungs, and also in the same amount of nitrous oxide as it escapes from the lungs.

The gases were, at a given temperature, passed through chloride of calcium to remove all the moisture, and then through caustic potassa to remove the carbonic acid. The amount of carbonic acid was ascertained by noting the excess of weight of the potassa after the addition of the carbonic acid.

Exp. a. In 18 cubic inches of air, we detected 0.165 grs. of carbonic acid, while from 18 cubic inches of nitrous oxide, under the same circumstances, we detected 0.700 grains of carbonic acid.

Exp. b. In 28 cubic inches of air was obtained 0.265 grs. of carbonic acid, while from 28 cubic inches of the gas was obtained 0.725 grs.

Exp. c. In 40 cubic inches of air 0.340 grs. of carbonic acid were found, while in 40 cubic inches of the gas 1.2025 grs. were found.\*

The air and gas were each caught in a rubber bag as they escaped from the lungs, and then at a temperature of 74° F. passed through the chloride of calcium and potassa.

\*I am indebted to Professor L. Stephens, of Girard College, for his kind assistance in obtaining these weights with great care and accuracy.

It will be noticed that the amount of carbonic acid obtained in experiments a and c, from the exhaled gas, is about four times the amount obtained from the exhaled air, while in exp. b it was but three times the amount. This apparent discrepancy is accounted for by the fact that at the last inspiration of gas in exp. b a breath of air was unconsciously taken into the lungs and breathed into the bag with the gas, consequently vitiating the experiment and giving a *much* smaller ratio of carbonic acid than in either of the other experiments.

Taking for granted, then, that we have an increased amount of oxidation, as shown by the excess of carbonic acid, let us now look at other important considerations.

#### STAGES OF ANÆSTHESIA.

In the production of anæsthesia by nitrous oxide gas we may very properly speak of three stages, viz :

1. The incipient stage, or stage of excitement, is that in which is felt a peculiar tingling or benumbing sensation in the periphery, and an acuteness of the senses, particularly the sense of hearing.

2. In the second stage there is a partial loss of sensation, palor of the face, muscular relaxation, and snoring.

3. In the third stage the respirations become slow and deep, and at times stertorous. There is a total loss of sensibility, both to pain and external impressions, deep palor of the face, with sometimes a livid appearance, and terminating with a subsultus tendinum. The average time required for the production of muscular relaxation and snoring is 50 seconds; 22.4 seconds elapse from the commencement of snoring to the subsultus of the muscles, and 37.8 is the average duration of anæsthesia sufficient to admit of an operation.

Children, aged persons and invalids, are, as a rule, the most susceptible to its influence. For a child of 3 or 4 years it requires only 15 or 20 seconds to produce anæsthesia. Females are also more susceptible to its effects than males.

## COLOR OF THE BLOOD.

It has been said by some writers that the blood during anæsthesia, by nitrous oxide, is of a dark color; and judging from the livid appearance of the face, in some cases, they have drawn the conclusion that the action of the gas is essentially asphyxia. Now, observation shows most conclusively that during the first and second stages, the blood is of a bright scarlet color, as it is also during the period of resolution or recovery, and there is nothing in the appearance of the patient, during these periods, that would indicate a different result. In fact, during the whole process the arterial blood is of a bright scarlet, while in the third stage, after the excessive oxidation has produced a temporary paralysis of the capillaries and a retardation of the circulation through them, we notice a darker color of the venous blood than is natural.

An apparent exception to this rule is sometimes seen in those cases where there is violent excitement and muscular contraction. In such cases the patient is partially asphyxiated, since the lungs are not receiving their due supply of breathing material. Such a condition is rarely seen and is generally caused by some peculiarity of dream. It is also much more likely to occur in subjects who are laboring under the effects of some narcotic at the time of inhalation, their narcotized condition preventing them from taking proper inhalations. If the blood flows from congested tissue, as for example, that about an inflamed or abscessed root of a tooth, if the patient breathe very sparingly of the gas as in the case above referred to, if the inhalations be persisted in beyond the third stage, or if the gas contain impurities, we shall then find the blood in the veins of a darker color. This fact may be readily understood, when we consider that after the production of anæsthesia by oxidation of the tissues, there is necessarily a retardation of the blood through the capillaries, and their peculiar narcotized condition, causing a retardation, prevents further oxidation.

## THE TEMPERATURE OF THE BLOOD.

The temperature of the blood increases slightly during the

process of anæsthesia, as might be anticipated, and as can be readily shown by placing a thermometer underneath the tongue during the inhalation and immediately subsequent to it.

#### COAGULATION OF BLOOD.

Blood flowing from wounds during anæsthesia, is seen to coagulate with rapidity. It often takes place so rapidly and forms so firm a clot, as to lead the patient who has submitted to the operation of tooth extraction, to suppose that his gums have been lacerated. These shreds of fibrin are among the best evidences that the gas acts by oxidation.

Every surgeon who has seen much of the operations of the gas must have noticed this remarkable tendency to coagulation as compared with the effects of ether or chloroform.

In 19,000 recorded cases where from one to a full set of teeth has been extracted, under my immediate supervision, there has not been one of immediately troublesome hæmorrhage, and not more than a dozen altogether, under any circumstances.

And in *these* cases, hæmorrhage has rarely occurred until from one to three days after the operation; and, in nearly every case the patient has been of a hæmorrhagic diathesis, as was evinced by the patient giving us the previous history; hæmorrhage having occurred in their own person or that of some member of the family, upon similar occasions in the past.

#### THE EXTREME LIMITS OF ITS ADMINISTRATION.

A Mouse lives in Nitrous Oxide,	from	30 to 60	seconds.
A Pigeon	" "	" "	1 to 2 minutes.
A Kitten	" "	" "	1 to 2 "
A Frog	" "	" "	30 to 60 "

The great diversity in time requisite for the destruction of life in the cases mentioned, is due to the fact that the frog being a cold-blooded animal, all the functions of animal life are performed with only a small fraction of the intensity which characterizes warm-blooded animals.

Man, judging from the appearance of persons in the third stage of anæsthesia, which is effected in from 30 seconds to two minutes, could not survive its inhalation for a longer period than from three to five minutes, depending upon the age, condition of health and susceptibilities to anæsthesia.

These conclusions, which have been reached by careful experiments, are widely different from some heretofore published.

For instance: Dr. R. Amory, of Boston, who has given the results of some very interesting experiments, to show the physiological action of the gas, gives the history of its effects upon warm-blooded animals, which had been confined in it for from 30 to 180 minutes, and gives the results of an autopsy in such cases.

Another experimenter, says: "I have frequently inhaled the gas for 20 minutes, the air being carefully excluded, without losing consciousness." Now, all such conclusions have been drawn from imperfectly performed experiments. The air in such cases could not have been entirely excluded. In one experiment by Dr. A. a pigeon lives 40 minutes; in a second, 84; and in a third, 32. Whereas, I have shown that if the animal be confined in pure gas, death ensues in from one to two minutes.

#### GASEOUS DIFFUSION.

The absorption of any gas by the membrane of the lungs, is materially modified by the law of gaseous diffusion.

Gases diffuse through any membrane or porous medium into each other with a velocity which is inversely as the square roots of their specific gravity.

For example: If one gas, with a specific gravity of one, be presented to one surface of an animal membrane, while a gas with a specific gravity of four be presented to the other surface, the velocities with which these gases will pass through the membrane will be to each other as two of the first to one of the second.

If the specific gravity of the two gases be the same, then the velocities of transfusion will be equal.

The following table gives the specific gravity, its square root, and the velocity of diffusion of Oxygen, Nitrous Oxide, and Carbonic Acid:

Specific Gravity.	Sq. Root of Spec. Grav.	Vel'ety of Diffusion.
Oxygen..... 1.10560	1.0515	0.9487
Nitrous Oxide..... 1.52700	1.2357	0.8200
Carbonic Acid..... 1.52900	1.2365	0.8120

If we take the velocity of transmission of carbonic acid as 1, that of oxygen will be 1.174; in other words, while one volume of carbonic acid is being eliminated from the lungs, there will be absorbed of oxygen, through the cell membrane, 1.174 volumes. This is nearly what we should expect to find if we make due allowance for other conditions which modify the action; one surface of the cell membrane being exposed to a gas, while the other is exposed to a liquid with a gas dissolved in it, or in a state of loose chemical combination with it. The volume of gas absorbed by a liquid is also modified by the pressure under which the gas above it remains after absorption has been completed.

The quantity of carbonic acid passing from the blood to the air cells would, therefore, depend on the one hand upon the excess of that gas condensed in the blood, and on the other hand upon the tension of the carbonic acid already contained in the air cells after having been eliminated from the blood.

The difference of permeability which animal membrane possesses for different gases must also modify the action and affect the result. Still, if we make due allowance for the oxygen that is disposed of by union with hydrogen and other elements of the animal organism, the above is about the ratio that we should anticipate.

Now, as the specific gravity of nitrous oxide and carbonic acid are almost exactly equal, their square roots are nearly the same, and they should, according to the above law, pass through the membrane of the lungs with nearly equal velocity.

But nitrous oxide is speedily soluble in water. It will, there-

fore, when exposed to the fluids of the body, be rapidly taken up and passed into the circulation.

By the laws of gaseous diffusion, then, we should look for an increased amount of carbonic acid in the exhalations from the lungs, while inhaling nitrous oxide, *provided* it be present in the blood in excess, for elimination; while on the other hand, if a diminished amount be present, we could not anticipate such a result. Now, in experiment b it has been shown that the amount of carbonic eliminated increases as the condition of anæsthesia approaches completion; in other words, its tension against the cell membrane is augmented, and the tendency to diffusion through the cell walls is increased as the process of anæsthesia progresses, a result which could not *possibly* have existed unless there had been during the production of anæsthesia an excess of oxidation. Moreover, if we examine the venous blood at the completion of anæsthesia, we shall find in it carbonic acid in excess of the normal amount, as explained elsewhere.

These facts taken in connection, if they do not prove, point conclusively, it seems to me, to oxidation as the cause of anæsthesia, while the retardation of the blood, together with its venous character in the third stage, are merely incidental effects.

#### RATE OF RESPIRATION.

Respiration is nearly normal during the first stage of anæsthesia; increased in force and frequency during the second; and slow, deep and full during the third.

Anæsthesia is produced much more rapidly if the breathing be vigorous, and the lungs well filled and emptied at each respiration, than it is if the respiration be slow and feeble; as, for instance, when 45 seconds were required by the first method, 75 seconds were required by the second.

Now, if anæsthesia were caused by a want of oxygen, as some authors assert, why should there be any difference in regard to time by the two methods mentioned, for in neither case is there any oxygen furnished, unless it be by the chemical decomposition of the nitrous oxide.

Experience has shown that the administration of the gas may, in all ordinary cases, be persisted in to the third stage without danger of accident, for although the patient is apparently at death's door, the instant the gas is removed and air is admitted to the lungs, a complete reaction ensues; we have an increased action of the heart, a flushed face, and in the course of two or three minutes the system resumes its normal condition.

The great safeguards in its use are the peculiar and unmistakable signs of the third stage, for while the patient is breathing deep and full at this stage, if any unfavorable symptoms become apparent, the gas can be instantly removed; the lungs fill with air, and in a moment the paralyzing effect upon the heart's action is gone, and the blood resumes its wonted circulation.

#### THE EFFECT UPON THE CAPILLARY CIRCULATION.

I have been able to ascertain the condition of the capillary circulation during the production of anæsthesia, by some experiments with frogs. They were placed in a bladder with one foot protruding in such a manner as to leave the bladder impervious to air. The web of the foot was placed under the microscope, and the condition of the circulation noted, and then by filling the bladder with gas, we were enabled to ascertain the effect upon the circulation during the different stages of anæsthesia.

For the first few minutes the movement of the blood seems to be but little affected. After from 10 to 15 minutes we notice that the force of the heart's action has been considerably increased, although the frequency has been but little changed, and in from 20 to 30 minutes the blood in the capillaries is seen to move along very slowly, until in the course of an hour, if the experiment be persisted in, the movement ceases entirely. Evidences of anæsthesia are seen before any diminution in the flow of blood through the capillaries, for the prick of a pin causes no movements of the frog, while yet the blood is moving with its ordinary force. Therefore it cannot be stasis of the blood in the capillaries which causes anæsthesia, for the stasis does not occur until several minutes after anæsthesia has been produced.

If we consider that the effect upon the circulation in the frog's foot takes minutes, while in warm blooded animals the same effect is produced in seconds, we shall have a pretty correct idea of the effect of the gas upon the circulation in man.

#### THE PURITY OF THE GAS.

The necessity of a pure article of gas has not, I think, been properly estimated by persons using it, or in other words, the danger of administering the gas in its impure state. Many persons who use it administer it immediately after it is made. I have been assured repeatedly by patients that they have waited at their dentist's office while the gas was being generated, and have taken it immediately afterwards. Now, all such gas contains impurities, even with the greatest care in the application of heat and washing of the gas.

If it be passed through several jars containing solutions for the removal of these impurities, it must be remembered that it passes through in bubbles of a globular form, and that it is only the outer surface of the bubble that comes in contact with the absorbing material, and consequently only a portion of the impurities can be thus removed.

The larger the number of jars used, the less will be the impurities found upon its exit; still, one has only to smell or taste the gas to find that such impurities are always present immediately after it is made. There will be found a slightly disagreeable odor and a brackish taste, and sometimes to such an extent are these impurities present that their inhalation is almost unendurable. The *patient* is not supposed to be able to detect these impurities while inhaling them, and unless the person administering the gas is aware of their presence, and is sufficiently conversant with them to be able to detect and eliminate them, he may be the innocent cause of an immense amount of injury.

These impurities may be traces of chlorine, the higher combinations of nitrogen and oxygen, or other impurities found in the nitrate of ammonia, used for the production of the gas.

No method in use will at once remove them all. If the gas be put into a gum bag, with a small amount of water, and thoroughly shaken for a few moments, after having passed through the wash bottles, it will be rendered nearly free from impurities. But it *ought*, in all cases, to be allowed to stand over a small quantity of water from six to twelve hours.

We shall then have a gas that is entirely non-irritating to the lungs, and so nearly like the air as scarcely to be distinguished by the person inhaling it. A small quantity of aqua ammonia injected into the gas, when first generated, will also assist very materially in removing the impurities, as it will dispose of the free chlorine, if there be any present, producing sal ammoniac, and will also, being an alkali, unite with any acids that may have been generated.

The gas too, if kept for several days, deteriorates to such an extent that it takes a much longer time for the production of anæsthesia, and ill effects follow, more or less, according to the condition of the patient's health at the time.

Complaints, of lassitude, headache, imperfect anæsthesia, and, of course, pains during the operation, are common under such circumstances.

The cause of this deterioration may be readily explained, although the *fact* is denied by many persons using the gas, upon the ground that it cannot pass through an air-tight metallic receiver.

All natural water contains in it not only air, but any other gases that may have been exposed to its absorption. If a jar of any gas be allowed to stand over water, upon the shelf of a pneumatic trough, it is first absorbed by the water, and then diffused into the air; at the same time the water absorbs the air and it is diffused into the jar. On account of this principle of diffusion, gases cannot be kept over water in a pure state for any length of time, and it is by this principle that we are enabled to explain the cause of deterioration in nitrous oxide, after standing over water even for two or three days; for it will not only contain air which has been diffused into it from the water, but any other gaseous impurities which the water contains.

It will be found necessary to continue the inhalations of gas that has been thus kept two or three times as long to produce anæsthesia as when it is pure, and sickness, nausea and other ill effects are quite likely to follow its administration in such cases.

That this principle of deterioration has been entirely ignored by many who use the gas, may explain the cause of the nausea and prostration which have sometimes been noticed to follow its administration.

As a rule we shall find that the sooner anæsthesia is produced in a given case, the more certain and agreeable is the gas in its effects.

It should also be generated at a temperature but little, if any, exceeding 400° F., or where a thermometer cannot be conveniently used, it should be allowed to boil very gently over a sand bath, so as to more equally diffuse the heat. A large retort is much preferable to a small one, for since the areas of surfaces are as the squares of their diameters, a retort of 12 inches in diameter has four times the evaporating surface possessed by one of 6 inches in diameter; consequently the heat is much more readily equalized, as the excess of heat is carried over rapidly in the vapor, thus preventing in a measure an increase of heat in the retort, and the danger of generating noxious gases. It must be remembered that if the temperature be elevated above a certain point, an opportunity is not afforded for the proper chemical changes to take place, and as a consequence, we obtain other gasses, the higher compounds of nitrogen and oxygen, which are irrespirable and poisonous to the system.

To appreciate the *ill effects* of such impurities, we have only to consider the fact that in a few seconds from the time the gas is taken into the lungs, its effects are felt sensibly in every part of the system.

As a matter of course, these impurities are carried instantly with the gas into the circulation, and produce their depressing and poisonous effects upon the system.

And, although a person of vigorous constitution and robust health may not receive apparent injury by the inhalation of such impurities, still the injury is none the less certain, while to a person in delicate health the pernicious influence may be speedily noticed.

I have been led to offer these suggestions because I believe it to be a very important consideration. I have been credibly informed of many cases where deplorable results have followed the neglect of these simple precautions in making and administering the gas.

In one case that came under my notice, the gas was made hurriedly, at a high temperature, and administered immediately to the patient, who came near dying upon the spot, and, I am assured, has never recovered her health, although nearly five years have elapsed since the occurrence. Such cases should not militate against the usefulness or safety of the gas when pure.

Many agents, effectually employed as medicines, when pure and unadulterated, act injuriously and are poisonous to the system under certain conditions. Even the food we eat may be of such quality, or may be taken in such quantity as to prove a poison instead of a nourishment.

#### ITS USE IN GENERAL SURGERY.

For minor surgical operations, the gas is undoubtedly by far the safest of anæsthetics, and with any proper degree of caution, it may be said to be absolutely harmless and efficient. It may be used in cases where the use of ether and chloroform are contra-indicated, on account of the debilitated condition of the patient, and in other cases where ether can only be administered with the greatest difficulty, owing to the attending excitement and muscular contraction.

Occasionally it requires from 15 to 20 minutes to etherize a patient, and there are strong arguments against its use in such cases, on account of the prolonged period of excitement to which the patient is subjected.

Now, in the use of nitrous oxide, anæsthesia is produced in less than two minutes from the commencement of inhalation. It produces not the slightest irritation of the mucus membranes. It causes no nausea or sickness. The recovery is complete in less than five minutes, and in most cases in less than three; provided, the inhalations have not been continued beyond the third stage. Anæsthesia lasts from fifteen seconds to one minute, sufficient for a short operation only, if it be the extraction of teeth or any operation about the mouth or nasal organs, but for other operations, its inhalation may be readily continued for several minutes, by allowing a frequent interchange of air with the gas. Still, unless a person has had considerable experience in its administration, it proves rather troublesome, even for a short operation, on account of the difficulty of entirely excluding the air during the inhalation.

I have frequently administered it for operations, lasting from three to five minutes, and have rarely found it objectionable, while, in most cases, it has worked admirably. One objection to its use is its bulk, and the consequent inconvenience of transportation, but if anæsthesia be required for not more than two or three minutes, a sufficient quantity can easily be carried in a gum bag of 10 or 12 gallons.

For long-continued operations, it would undoubtedly save an immense amount of sickness, and, being unattended with the dangers of chloroform and ether, it would prove a great blessing to humanity; but, unfortunately, the difficulty attending its administration in such cases is the great barrier to its use.

If the patient be susceptible to the influence of anæsthetics, it will answer the purpose admirably; but, since there must be a constant interchange of air with the gas, and because its effects upon some persons are so transitory, passing off in a few seconds, the difficulty of administering it in such cases has rendered it unavailable in protracted operations.

It is nearly *impossible*, in some cases, where great excitement and muscular contractions are produced, to entirely exclude the air, even for a short operation.

I recall one case in particular, in which the only alternative

was to hold the patient by force, or desist from the attempt at anæsthesia altogether, even for a momentary operation.

The same difficulties had to be encountered at each of the four attempts at anæsthesia.

The lady was very anxious to have her teeth extracted, and, after two attempts and failures in the ordinary manner, at her request, she was held quiet until the period of excitement was passed. She proved a very susceptible patient after the excitement was over, anæsthesia lasting as well as usual.

Dr. Broadbent, of the *British Medical Review*, June, 1868, says: "From the fact that in order to obtain insensibility without excitement, Nitrous Oxide must be given unmixed with air, it is probable that it acts simply by preventing access of Oxygen to the nervous-centres."

Now, the case just cited as well as hundreds of others that could be adduced, prove conclusively the fallacy of his reasoning.

There is always a period of excitement, although not manifest to the observer, in all cases, its action being the same as that of other stimulants.

A difference in temperament, together with the fact that the patient passes through the stage of excitement in a few seconds, his mind being occupied meanwhile by the peculiar sensations, or by what may be said by the one who administers the gas for the purpose, may explain the absence of any appearance of excitement in many cases.

For oftentimes if a movement be commenced by the patient, the excitement manifests itself, and is sometimes almost uncontrollable. Some remark made by a bystander, or a noise from the street, may be all that is necessary to show that, although the patient is quiet and appears to be laboring under no excitement, still the very opposite of this is the case.

#### ITS SAFETY.

Its use has become so general for short surgical operations, particularly the extraction of teeth, &c., that the question of its

safety has become one of vital importance. Every medical practitioner has seen more or less of its injurious effects as administered by persons ignorant of the simplest principles of chemistry, as well as of its physiological action, and I doubt not it is often a source of anxiety to know just when to advise its use, and when its use is contra-indicated.

I may premise by stating that, in my own experience, it has rarely been found injurious, even for a person in delicate health, to inhale a sufficient amount to admit of a momentary operation, while at the same time I have frequently met with patients to whom I should not care to administer it for a protracted operation.

In less than one per cent. of the cases operated upon, has there been any nausea or sickness following. In fact, there is never any trouble of the kind if the patient is in tolerably good health at the time of inhalation.

The most unfavorable conditions are a bilious state of the system, a long abstinence from food, or sickness at the stomach. In cases like the above, there is a strong probability of nausea and vomiting, especially if the administration be persisted in beyond the commencement of the third stage, although this condition is commonly relieved by vomiting. I have occasionally seen a patient in such a condition inhale the gas, when emesis followed, which gave entire relief, so that after a few moments a second inhalation produced no ill effects whatever, and such a patient has left the office declaring he felt better than when he came.

To avoid nausea in similar cases, the gas should be administered as sparingly as possible for the operation; and in general, I would advise that the operation be as short as possible to relieve present suffering, deferring the balance until the system of the patient be in a more healthful condition; for practical experience in my own person, as well as with others, has fully convinced me that one may inhale the gas in moderate quantity, daily for weeks or months together, without harm.

## ITS SAFETY IN DISEASE.

Is it safe in the various organic diseases, such as the heart, lungs, brain, &c.? Thousands of invalids have suffered torture for months and years because they dreaded the surgeon's knife, and in like manner, other thousands suffering from some organic or functional disorder of the system, have dreaded the dentist's forceps, and fearing to take an anæsthetic, have for years carried in their mouths a mass of filth, a fruitful cause of disease, which has not only ruined their health and destroyed their happiness, but made them objects of repugnance to all who are so unfortunate as to be associated with them.

If the above question can be answered in the affirmative; if nitrous oxide is safe for such afflicted ones, it is, certainly, a great boon to suffering humanity.

Having used it almost indiscriminately for the past five years, I present below the results of my experience :

DISEASE OF LUNGS.—It is a well-established fact that pure nitrous oxide gas is entirely non-irritating to the lungs, and as we have already shown, its action upon the blood, is to increase the property of coagulation. A person who is predisposed to hæmorrhage can inhale the gas with entire immunity from danger—indeed, I think with less danger than would attend the operation if no anæsthetic were administered, since the shock to the system is thereby avoided, and there is but a slight increase in the force of the circulation. In a large number of such cases where the gas has been administered for tooth-extraction, I have never met with one where any hæmorrhage followed immediately succeeding the operation, nor any in which the after effects proved unpropitious; and this, notwithstanding a large number have had hæmorrhages previous to the operation, and some immediately preceding it. I should state here that, in all cases of disease, the effects of the gas are watched with the greatest care, and if any untoward symptoms present themselves, it has been discontinued, although this has never, in a single case, been found necessary until the patient was sufficiently under its influence

to permit of a momentary operation; as for instance, the extraction of a tooth.

**HEART DISEASE.**—In this disease the effects should be watched with care, and there will be no danger. The cumulative action of the gas is only for a few seconds, so that if it be withdrawn at any time during the process, a reaction takes place in a moment, we might almost say before the patient has time to die; while with ether and chloroform there is a cumulative action for from 20 to 50 seconds after they have been discontinued, and several minutes may elapse before consciousness returns. Although its evanescent character is a great obstacle to its use for long operations, still, that is the great safeguard against accident, for the heart's action may be under your control, as the engine is under the control of the engineer. If the pressure is too great, he lets off the steam; if the heart's action is either increased or diminished inordinately, remove the gas and in a moment it resumes its wonted action.

In two recorded cases the condition of the patient was so critical that I should scarcely have dared to extract a tooth without the use of an anæsthetic, fearing the shock to the system incident to the operation, there being in one case a complexity of diseases, hypertrophy, dilation and valvular disease, which had been continued for 12 years. He had formerly followed the sea, but had not been able to go upon the streets, without assistance, for several years. He was pale and anæmic, with an irregular and intermittent pulse.

The administration of the gas was continued only to near the close of the second stage; the patient recovered without any untoward symptoms, and left the office in a few moments declaring he felt better than when he came in. He certainly looked much better, having lost that deathly palor of face which he had when he sat in our operating chair. The danger in such cases is that the feebleness of the heart's contractile power may cause its action to cease altogether, during the period when this power is partially destroyed by the paralyzing action of the anæsthetic, while the safety lies in the instantaneous reaction after the withdrawal of the gas.

In CHOREA, HYSTERIA, EPILEPSY, and other diseases dependent upon a disordered condition of the nervous system, it is productive of no bad results, unless it be pushed too far; while if only the second stage of anæsthesia be produced, so that it shall act as a stimulant to the nervous system, and not a depressing agent, it will in many such cases prove a most valuable remedial agent.

Uncomplicated Neuralgia is oftentimes instantly relieved. I could adduce a hundred instances of the kind, where the patient has sat down with a severe headache, and been entirely relieved by a few inhalations of the gas. On the other hand, if a disordered condition of the stomach cause the neuralgic pains, instead of proving a relief, it will only aggravate the trouble.

A lady who had inhaled ether a half hour previously, for the extraction of some teeth, and had been unsuccessful, came to the office with a severe headache; she inhaled the gas, her teeth were drawn, and upon recovery she stated that her headache was entirely relieved.

HYSTERIA.—The gas, by its stimulating action upon the nerves, has oftentimes proved beneficial in cases that have come under my observation.

Such patients generally leave the office with hysterical symptoms much less aggravated than before the inhalation. During the operation, the friend in attendance sometimes expresses fears that the patient may have one of her "nervous spells," noticing some contortion of the face or movement of the hand as she is waking from a dream, but in a few moments, as soon as complete recovery has taken place, there is usually a calmness of the patient, quite surprising to the attendant, she being able to write her name with as steady a hand as usual, within five minutes of the commencement of inhalation.

I have the record of an interesting case of a young lady, who had not been able to speak above a whisper for several months previous to taking the gas, who a few days subsequent called and informed me, with the greatest delight, that she had been cured, as she could talk now as well as ever.

The fact that she awoke after the operation crying out, may have had some agency in effecting the cure, as she thus learned that she possessed vocal organs and could use them.

Still, this case in connection with very many others of a like character, has convinced me that pure nitrous oxide may be employed with great advantage in cases of hysteria; while, on the other hand, if it be impure, either on account of its being prepared so recently, or for too long a period, or, if persisted in beyond the third stage, it is absolutely injurious.

**ASTHMA.**—Asthmatic patients express a sense of relief after inhaling the gas, which in some instances, at least, seems to be of a permanent character. A gentleman of sixty years, whose disease was inherited and who had been a severe sufferer for many years, was almost entirely relieved for a whole winter by inhaling for a few successive days, once or twice each day, a quantity sufficient to produce the second stage of anæsthesia, although he had not been free from the disease, at this season of the year, for about twenty years.

**PARALYSIS.**—Quite a number of patients afflicted with paralysis in a greater or less degree, have come under my observation, upon whom the gas has had a very pleasing effect, in stimulating the nervous system to action, and thus restoring the tone of the paralyzed parts, more or less completely.

One such case was that of a gentleman who had, for a long time, been afflicted with paralysis of the bladder. He inhaled the gas upon several occasions, for the relief of neuralgia. After a few inhalations, the paralyzed condition was much improved, as was evinced by his freedom from incontinence. It is necessary in such cases to produce only the second stage of anæsthesia.

**EPILEPSY.**—The following cases of epilepsy are of considerable interest:

*Case 1.*—A young man, 28 years of age, who had inherited the disease, inhaled the gas for six weeks, two or three times in

a week. During the first week, he had three epileptic attacks; during the second week, two; during the third, one, and for the three weeks succeeding, not any.

I presented the case, at the time, at the University clinics, but have never been able to obtain its subsequent history. Previous to inhaling the gas, he had had two or three attacks daily, and he had not been free from them for so long a time, for several years. Two years previously, he had inhaled the gas for tooth extraction, with a favorable result, which he at the time attributed to the bromide of potassium, which he was taking.

*Case 2.*—A young lady inhaled the gas as a remedy in the same disease. She recently informed me that she had not had an attack for several months, although before this she had experienced them frequently. She attributes her freedom from attacks to the remedial efficacy of the gas.

We will now make a brief comparison of the relative effects upon the system, of Oxygen, Nitrous Oxide, and Carbonic Acid.

#### OXYGEN.

In the respiration of pure oxygen, we have, at first, a rapidity of pulse, increased number of respirations, and an increase of temperature. The animal suffers little or no inconvenience for an hour or so, but symptoms of coma gradually present themselves, and death ensues in six, eight, ten or twelve hours.

If the animal be removed into the air before the insensibility is complete, it quickly recovers.

The blood is of a bright scarlet color, and coagulates with remarkable rapidity, and it is to alterations in its character occasioned by hyper-arterialization that we are to attribute a fatal result.

There can be no doubt that an undue amount of oxygen is absorbed, and it does not seem unlikely that one cause of death is the stagnation of the blood in the systemic capillaries conse-

quent upon the want of a sufficient change while passing through them.—*Carpenter's Physiology.*

#### NITROUS OXIDE.

In the respiration of Nitrous Oxide, as in the case of Oxygen, we have an increase in the force of the heart's action, respirations more rapid, temperature elevated, no signs of distress, or discomfort while breathing it, and death ensues in a few minutes instead of hours, owing, probably, as has already been suggested, to the intense avidity with which the oxygen seizes upon the tissues when in its nascent state, just at the moment of liberation from its union with nitrogen.

If the inhalations be discontinued before fatal symptoms become manifest, the patient immediately recovers without having suffered any inconvenience. The blood is of a bright scarlet color during the first stages of anæsthesia, but if the inhalations be persisted in beyond the third stage, until the whole system becomes paralyzed by the excessive oxidation, we then have a diminution in the power of the heart's action, a retardation in the flow of blood through the capillaries, and the venous blood becomes more or less loaded with carbonic acid.

There is no venous congestion such as is consequent upon a deprivation of oxygen.

This retardation of the blood may be produced by any agency which alters the chemico-vital relations between the blood and the tissues which it permeates.

Thus the application of a stimulant, as, for example, the electric current, to the capillaries causes the blood corpuscles to adhere to each other and to the walls of the vessels, producing friction and a consequent retardation, and finally, a total stagnation of the blood. A stream of carbonic acid injected against the capillaries, or a depression of the vitality of the part by such injuries as tend to excite inflammation in it, also produce a like stagnation.

The retardation produced by the inhalation of nitrous oxide does not take place until the third stage of anæsthesia. It

cannot, therefore, be considered the *cause* of anæsthesia, but is rather a *result* of the paralyzed condition of the capillaries.

This fact was demonstrated by the microscopical examination of the circulation in the foot of a frog during the production of anæsthesia.

As a further proof of this fact, let a full inhalation of nitrous oxide be taken, and we shall feel a peculiar tingling or benumbing sensation in the peripheral extremities, very sensibly, in from five to ten seconds, much sooner than any evidences of retardation of the circulation are noticed.

For an illustration, allowing that the blood reaches the capillaries of the fingers in five seconds after it leaves the lungs (a result we might anticipate, calculating the rate of movement at 12 inches per second), we shall perceive its effects, almost instantly, upon its arrival there.

Now we have already shown that there is a largely increased amount of oxidation, and it is but fair to conclude from the suddenness of its effects, that it is the *cause* of the peculiar sensations which we denominate the commencement of anæsthesia, and also, the cause of the retardation.

We should also anticipate a retardation the same as when pure oxygen is inhaled, only in a much less space of time. A noxious agent or poison might produce a retardation of the blood, or it may be a total stagnation, but nitrous oxide is *not a noxious agent*, therefore, if it does not act by oxidation, it merely prevents access of oxygen to the brain. Its action cannot be by the latter method, since the time requisite for its operation is altogether too limited.

#### CARBONIC ACID.

The most prominent symptoms, as the result of the inhalation of carbonic acid, are a distressing sense of a want of breath, consequent upon the presence of unchanged venous blood in the capillaries of the lungs, as also probably in the systemic capillaries.

There is anxiety of countenance, intense expression of distress,

quick and violent movement of the respiratory muscles, and a decrease of temperature. The chest heaves, the shoulders are elevated, the *alæ nasi* are dilated, and the patient throws himself about convulsively. The face assumes a livid hue, the lips are of a dark purple color, the veins are distended and the eyes prominent. The blood is found to be more fluid and less coagulable. As the imperfectly arterialized blood exerts more and more its depressing influence upon the nervous-centres, they become completely paralyzed and respiration ceases.

The heart's action finally ceases, owing to two distinct causes: 1, an undue distension of the walls of the right ventricle; and 2, to a deficiency of stimulus to excite to contraction the walls of the left ventricle.—*Wood's Practice*.

Now, if the action of nitrous oxide be similar to that of carbonic acid, producing anæsthesia by asphyxia, or if its effects were caused by a stasis of the blood in the capillaries, we should have in either case a decrease of temperature, owing to a deficiency of oxidation.

We should also find the blood in a more fluid condition than in its normal state: while, on the contrary, we find an increase in temperature, and the blood richer in oxygen.

The action of both oxygen and nitrous oxide is to increase the force of the heart's contractions, to redden the blood globules, and they are both stimulants to the medulla oblongata; while carbonic acid, on the other hand, acts as a poison, destroying the proper action of the heart and brain, and it *must* be continually eliminated. It also suspends the respiratory functions by its depressing action upon the nervous centres.

We notice from the above comparison, the great similarity of action between Oxygen and Nitrous Oxide, and the dissimilarity of action between either of these and Carbonic Acid.

#### GENERAL CONCLUSIONS.

I. It has not been my purpose, in speaking of the therapeutical value of nitrous oxide, to say more than merely to *hint at* what has been my experience in certain cases that have come, *incidentally*, under my observation. I am satisfied, also, that in *some instances*, at least, the results obtained, when I have used

it for medicinal purposes, were not as satisfactory as could have been desired, simply because at that time its *modus operandi* was not sufficiently understood, and its administration was pushed too far, so that instead of acting as a stimulus, it proved a source of debility.

II. I have often noticed that a few breaths of the gas have occasioned an agreeable sense of relief from the *ennui* caused by the heat of summer, such a result as might have been anticipated from breathing an atmosphere richer in oxygen.

Other proofs of oxidation are as follows, viz :

1. An increased amount of carbonic acid generated.
2. The scarlet color of the blood during the first stages of anæsthesia, as well as during the period of resolution.
3. The coagulability of the blood during and subsequent to anæsthesia.
4. An increase of temperature during the production of anæsthesia.
5. The general similarity of its effects as compared with pure oxygen.

III. Its remarkable power and rapidity of action, as compared with oxygen, are owing to the oxidation taking place just at the moment of its liberation from union with nitrogen, while in its nascent state.

IV. Its safety, momentary reaction, and agreeable after-effects, are due to the fact that, acting as an oxidizer, the products of its combinations are speedily eliminated from the system.

V. A sufficient proof of its innocuousness, when pure and properly administered, is found, in the fact that so many thousands of persons, in almost all conditions of health, have inhaled it without any fatal accident, and with less disturbance to the system than would have resulted from an operation without the use of any anæsthetic. Many a patient who has fainted at the touch of a sensitive tooth, has taken the gas immediately after for the extraction of teeth, without the slightest disturbance to the system.

VI. No tendency to syncope follows the inhalation of *pure* gas. While if it be *impure*, either because it has been generated too recently, or at too high a temperature, or because of standing too long over water, it cannot be taken with impunity.

VII. While it answers the purpose admirably for short surgical operations, it cannot be used *indiscriminately* for long continued operations.

VIII. The rapidity with which it will paralyze the whole capillary system, as well as the heart's action, stopping respiration and destroying life, show that, although harmless when properly administered, it is *powerful for evil*, unless its action and effects are *thoroughly understood*.

IX. The *paucity of fatal accidents* attending its administration, and its *harmlessness* as compared with ether and chloroform, are due to the striking characteristics of the *fatal symptoms*, and to the *rapidity of the reaction which follows* its inhalation. So long as the breathing is like that of a person in deep, natural sleep, there is no immediate danger, but if there be signs of interruption of the respirations, and a cadaverous or livid countenance, the gas should be *instantly discontinued*. These are the *main indices of danger*.

X. It does not act by asphyxia, since there is no venous congestion, and its effects are too speedily felt to be produced by a want of oxidation. If this were its *modus operandi*, we might anticipate the same results from the inhalation of nitrogen. A *marked difference* between its effects and asphyxia is noticed when, from any cause, the patient while inhaling it omits to take free inhalations of the gas.

XI. It is undoubtedly a very valuable remedial agent, *especially* in certain diseases dependent upon a disordered condition of the nervous system. When used for such purposes, it should be given in small doses, ordinarily, only to the commencement of the second stage.

XII. The debility which *sometimes* follows its administration is due either to its being persisted in to the third stage, or to a disordered condition of the digestive system at the time of inhalation.

One of the most *unfavorable indications* for its administration is in *hyperæmia* of the liver. In such case *nausea* is very likely to ensue, caused, as might be anticipated, from a retardation of the blood. In certain organic diseases of the brain, whether acute or chronic, it is also entirely inadmissible in quantity sufficient for the production of anæsthesia.

From a record of cases, which I am at present making, I hope, at some future time, to be able to present a more full and complete history of the effects of nitrous oxide upon the system, in its diseased conditions.



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